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Post-cesarean analgesia: quo vadis?

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"Any man can be a father, but it takes a special person to be a dad."
Proverb
This work is dedicated to the loving (and never fading) memory of my Father Marian Kuczkowski who lost a battle with cancer in Lodz, Poland on April 30, 1985.
Krzysztof M. Kuczkowski, San Diego, California, November 5, 2009

Summary

There is currently no "gold standard" for post-cesarean pain management. The number of options is large and the choice of the method of pain control is determined by drug availability, institutional protocols, individual preferences, available resources and financial considerations. This article provides an overview – the state-of-the art - of the currently available methods of post-cesarean analgesia. *Anestezjologia i Ratownictwo 2010; 4: 296-303.*

Keywords: pregnancy, obstetric anesthesia, cesarean section, postoperative pain control, pain management; acute pain management

Changing horizons of modern anesthesia practice

In the new millennium, the horizons of modern anesthesia practice continue to expand beyond the provision of surgical anesthesia to encompass areas outside of the operating room, including preoperative evaluation, labor analgesia, postanesthesia care, critical care and pain management [1]. Thus a fundamental aspect of the practice of anesthesiology, the prevention of intraoperative sensation (including sensation of pain) continues to expand into postoperative prevention and treatment of acute pain and prevention and treatment of chronic pain in pain clinic [2].

Obstetric anesthesia in the new millennium

The subspecialty of obstetric anesthesia presents a spectrum of challenges to the anesthesiologist not only in provision of acute intrapartum labor analgesia (acute intrapartum pain management), or surgical anesthesia for abdominal delivery, but also in provision of postoperative analgesia (acute postoperative pain management) [3]. It has been well established that postoperative pain leads to patient discomfort, decreased level of satisfaction, prolonged recovery and higher health care cost. Specifically in the parturient inadequate postoperative pain control after cesarean section may interfere with ambulation, breast-feeding

and early maternal bonding with the infant [4].

Obstetric pain: an emotional and sensory experience

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage" [1,4]. All cultures throughout history of humankind have attempted to control pain. Postoperative pain is a potent trigger for stress response, activates the central nervous system, and is thought to be an indirect cause of adverse effect on various organ systems. During the management of postoperative pain, the physician must balance the degree of pain relief with avoidance of undesirable side effects [1]. The effective pain management does not necessarily make the parturient totally insensible to the fact that abdominal surgery (cesarean section) was performed, but rather, it allows adequate degree of comfort and promotes physical recovery and a sense of well being [4]. Effective postoperative analgesia can be provided with systemic administration of opioids and/or nonopioid analgesics as well as with epidural and spinal techniques [5-13].

Several studies have demonstrated that patient education increases the efficacy of systemic opioid analgesic techniques after cesarean section [1,4-7]. Parturients should understand the importance of effective pain control, and they should receive instruction in the use of patient controlled delivery systems. While many parturients present with a significant amount of prior knowledge regarding labor analgesia, others may have little or no understanding of the labor and delivery and pain relief options, including postoperative pain control.

Systemic opioids and breastfeeding

There is little objective information on the effect of systemic opioids administered to the mother on her breastfeeding newborn. Drug excretion into human milk may occur when a drug binds to the milk proteins or adheres to the milk fat globules. Several factors including timing of breast-feeding (relative to drug administration), and breast milk contents influence drug excretion into human milk [14,15]. Lipid soluble drugs are more likely to accumulate in mature milk (which has higher fat content) than in colostrum. Likewise, opioids, most of which are weak bases are more likely to accumulate in mature milk than in colostrum. The American Academy of Pediatrics Committee on Drugs lists morphine, fentanyl and butorphanol as maternally administered opioids that are compatible with breast-feeding [14]. The British National Formulary guidelines advise that therapeutic doses of morphine given to the mother are unlikely to affect the newborn [1]. A parturient may safely breast-feed while receiving systemic opioid after cesarean section. However, the newborn should be evaluated for signs and symptoms of systemic drug transfer and accumulation [4].

Pain control after cesarean section

In the United States most cesarean sections are performed under regional anesthesia, and the administration of subarachnoid or epidural opioids has become a popular technique for postoperative analgesia [1,4]. It has been reported that more than 90% of obstetric anesthesiologists administer subarachnoid or epidural opioids in parturients undergoing cesarean section under spinal, epidural or combined spinal epidural anesthesia [1,4,7,11]. Administration of subarachnoid or epidural opioids offers several advantages to parturients recovering from cesarean section. These include excellent postoperative analgesia with a decrease in total dose of opoioid required, a low level of sedation, minimal accumulation of the drug in breast milk, facilitation of early ambulation and early return of bowel function [7,11]. Pruritus is the most common side effect of neuraxial morphine administration, and it is the most frequent cause of patient dissatisfaction with this technique. Delayed respiratory depression is rare but serious complication that results from extreme cephalad migration of the opioid (morphine) to the brain stem through the CSF [4].

Historically, the obstetrician has prescribed postoperative pain medications when writing the general postoperative orders. However, in the last decade increased perception of the role of an anesthesiologist as a vital member of the peripartum care team has shifted more responsibility on members of our specialty, including provision of postoperative analgesia [1]. Several factors contribute to the increasing involvement of the anesthesiologist in acute postoperative pain management. These include profound knowledge of the physiological changes in pregnancy, knowledge of neuroanatomy, understanding of pain pathways, physiology and the mechanism of pain, knowledge of pharmacology, pharmacokinetics and pharmacodynamics of analgesic drugs, and skills in regional anesthesia.

Despite attempts to improve postoperative management of pain, a significant number of patients (including parturients) continue to experience inadequate postoperative analgesia resulting in distress, increased morbidity and prolonged hospitalization [4]. Although administration of opioids still remains the pillar of postoperative treatment of severe pain, a better understanding of the pathophysiology of pain is allowing clinicians to introduce a more balanced multimodal approach to postoperative analgesia [5-13]. The development of multimodal approach to postoperative pain control provides high quality postoperative analgesia with minimal side effects.

Quality of anesthesia and postoperative outcome

The exact relation between quality of analgesia and postoperative outcome still remains ill defined, and there is some evidence that relief of pain per se may play only a limited role in attenuation of postoperative physiologic responses and morbidity [1,4]. Several studies have demonstrated the superiority of nuraxial postoperative analgesia as compared to systemic opioids either administered as a single bolus or a patient controlled modality [5-13]. To potentiate and prolong the effect of epidurally administered opioids, combinations with local anesthetic have been used [4]. The addition of local anesthetics improves the quality of postoperative analgesia and enables the reduction of opioid requirements. Another viable option for postoperative pain control is the combination of opioids with clonidine and epinephrine [10-12]. The development of never and injectable non-steroidal anti-inflammatory drugs (NSAIDs) initiated several studies in which NSAIDs were used alone or in combination with other analgesic techniques for pain relief after cesarean section [4]. It remains unclear whether NSAIDs are equally effective as compared to neuraxial postoperative analgesia or should rather be combined with such techniques to improve the analgesic quality.

Postoperative pain control: an evidence based approach

Vercauteren et al. compared the analgesic effect and cost-effectiveness of intrathecal morphine and PCEA after cesarean delivery [6]. The authors concluded that PCEA offered better analgesia with less nausea and vomiting than intrathecal morphine, but was more expensive, primarily due to the PCA equipment [6].

Draisci et al. conducted a prospective, randomized, double blind, controlled trial in which the authors compared the effects of co-administration of intrathecal sufentanil and morphine with intrathecal sufentanil and a single administration of subcutaneous morphine [7]. Sixty-four pregnant women scheduled for elective cesarean section under spinal anesthesia were assigned to two groups according to the way of administration of morphine: intrathecal sufentanil (5 microg) plus intrathecal morphine (150 microg) (ITM group), and intrathecal sufentanil (5 microg) plus single administration of 10 mg subcutaneous morphine (SCM group). In both groups, the local anesthetic used was hyperbaric bupivacaine 0.5 percent (10 mg). In the postoperative period, pain was recorded on a 0-100 visual analog scale (VAS) and intravenous tramadol (100 mg) was administered if VAS score was >40 mm. Collateral effects, such as nausea, itching, respiratory depression, and sedation were assessed. VAS scores at rest and on coughing were significantly higher in the SCM group than in the ITM group between 3 and 24 hours [7]. The mean titrated dose of tramadol consumed was also significantly greater in the SCM group than in the ITM group ($p < 0.05$). The time to first administration of tramadol was lower in the SCM group versus the ITM group ($p < 0.05$). The incidence of nausea was significantly lower in the SCM group than in the ITM group ($p < 0.05$). There was no significant group difference in the incidence of pruritus ($p > 0.05$). The authors concluded that co-administration of sufentanil and morphine into the subarachnoid space was effective and provided longer pain relief than intrathecal sufentanil plus a single injection of subcutaneous morphine, despite a higher incidence of side effects such as nausea and vomiting [7].

Bamigboye et al. conducted a chart review study designed to assess the effectiveness of surgical wound infiltration with local anesthetics and/or abdominal nerve blocks on post-cesarean section pain control [8]. Parturients who underwent cesarean section under neuraxial blocks and received surgical wound infiltration with local anesthetics reported decreased morphine consumption at 24 hours postoperatively compared to parturients who received placebo. In women who underwent cesarean delivery under general anesthesia with abdominal wound infiltration (and peritoneal spraying with local anesthetics) the need for postoperative opioids was also reduced. The numerical pain score (0 to10)

within the first hour after the surgery was also reduced [mean difference (MD) -1.46; 95% CI -2.60 to -0.32]. Parturients in regional anesthesia group who received NSAIDs and wound infiltration with local anesthetics consumed less morphine (MD -7.40 mg; 95% CI -9.58 to -5.22) compared to local anesthetic control alone group. Women who received regional anesthesia with abdominal nerves blocked also reported decreased opioid consumption (MD -25.80 mg; 95% CI -50.39 to -5.37). Addition of ketamine to the local anesthetics surgical wound infiltration in regional anesthesia group did not confer any advantages [8]. The authors concluded that surgical wound infiltration with local anesthetics and abdominal nerve blocks (as adjuncts to regional and general anesthesia) are of benefit in postoperative pain control after cesarean section (by reducing postoperative opioid consumption).

Benhamou et al. conducted a 26-item survey questionnaire (organization of the maternity unit, preoperative evaluation, technical aspects describing regional or general anesthesia, oxytocic and antibiotic drugs, postoperative analgesia) which was distributed to all French obstetric units (excluding overseas) [9]. The response rate was 73% (451/621). Preoperative evaluation included a recent platelet count in 97% of responding units, and information was given to patients in 84% of cases. Antibiotic prophylaxis in accordance with French guidelines was used in 78% of units. Anesthetic techniques were single-shot spinal, epidural, combined spinal epidural and general anesthesia in decreasing order (92.5, 4.5, 2 and 1%, respectively). Effervescent cimetidine was the first choice in 62% of units. Cricoid pressure and succinylcholine were routinely used in 66 and 77% of units, respectively. Oxytocin was used appropriately in 65% of units. In addition to spinal or epidural opioids, paracetamol, NSAIDs and nefopam were added postoperatively in 98, 68 and 19% of units, respectively [9]. Poorer practices were found in units having a lower annual delivery rate. The authors concluded that overall practice was in accordance with national guidelines or practice patterns defined by the expert committee. Regional anesthesia and postoperative analgesia-related techniques particularly were adequate. Some deficits were of limited importance (antibiotic prophylaxis and oxytocin administration), whereas others (use of succinylcholine and cricoid pressure) remain of concern [9].

Lavand'homme et al. evaluated the postoperative antihyperalgesic effect of intrathecal clonidine after cesarean delivery [10]. The study included ninety-six parturients undergoing elective cesarean delivery who were randomly assigned to receive intrathecal bupivacaine-sufentanil (BS group), bupivacaine-sufentanil-clonidine 75 microg (BSC group), or bupivacaine-clonidine 150 microg (BC group). The primary outcome was the extent and the incidence of peri-incisional punctate mechanical hyperalgesia as assessed by response to application of a von Frey filament at 24 and 48 h after cesarean delivery [10]. Postoperative morphine requirements and pain scores, as well as residual pain at 1, 3, and 6 months, were also assessed. The BC group had a significantly reduced area of peri-incisional hyperalgesia at 48 h (median, 25th-75th percentiles): 1.0 (1.0 - 3.3) cm (2) vs. 9.5 (5.0-14.0) cm [2] in the BS group vs. 5.0 (2.5-12.3) cm [2] in the BSC group (P = 0.02 with the BS group). The incidence of hyperalgesia at 48 h was also lower in the BC group: 16% vs. 41% in the BS group vs. 34% in the BSC group (P = 0.03 with BS group). Postoperative morphine consumption, pain scores, and incidence and intensity of residual pain did not differ among groups [10]. The authors concluded that intrathecal clonidine 150 mug combined with bupivacaine had a postoperative antihyperalgesic effect expressed as a significant reduction in the extent and incidence of peri-incisional punctate mechanical hyperalgesia at 48 h after elective cesarean delivery compared with intrathecal bupivacaine-sufentanil and intrathecal clonidine 75 mug-bupivacaine-sufentanil [10].

Carvalho et al. conducted a study designed to compare postoperative analgesic consumption, pain scores and side effects of extended-release epidural morphine (EREM) with conventional morphine for the management of post-cesarean pain in a setting more reflective of current obstetric practice [11]. Seventy healthy parturients undergoing elective Cesarean delivery were enrolled in this randomized, double-blind study. Using a combined spinal epidural technique, patients received an intrathecal injection of bupivacaine 12 mg and fentanyl 10 mcg. After closure of the fascia, a single-dose of either conventional morphine 4 mg or EREM 10 mg was administered epidurally. Postoperatively, all patients received ibuprofen 600 mg orally every 6 h. Oral oxycodone and IV morphine were available for breakthrough pain [11]. All patients received pulse oximetry and respiratory monitoring for 48 h post-cesarean delivery. Single-dose EREM significantly improved pain scores at rest and during activity. The median (interquartile range) of supple-

mental opioid medication usage for 48 h post-cesarean (in milligram-morphine equivalents) decreased from 17 [22] to 10 [17] mg with EREM compared to conventional epidural morphine (P = 0.037). Both drugs were well tolerated with no significant difference in adverse event profiles [11]. The authors concluded that EREM provides superior and prolonged post-Cesarean analgesia compared to conventional epidural morphine with no significant increases in adverse events [11].

van Tuijl et al. studied the effect of addition of intrathecal clonidine to hyperbaric bupivacaine on postoperative pain and morphine requirements after cesarean section (a randomized controlled trial) [12]. A group of 106 women received spinal anesthesia using either bupivacaine 0.5% (2.2 ml) heavy with 0.5 ml normal saline 0.9% (B) or bupivacaine 0.5% (2.2 ml) heavy with clonidine (75 microg) in 0.5 ml normal saline 0.9% (BC). The primary outcome was the total morphine consumption in the first 24 h after surgery. Secondary outcomes were the duration of postoperative analgesia, postoperative pain scores, and the need for alfentanil during surgery, block regression, clonidine side-effects and morphine side-effects [12]. Total morphine consumption was similar in both study groups. The mean time to the first analgesic request in the BC group was 129 (SD 13.8) min, compared with 55 (14.2) min in the B group [mean difference (95% CI) -75 (-106 to -44) min]. In the BC group 22 (42%) patients had a complete motor block 1 h after surgery compared with 4 (8%) patients in the B group [RR (95% CI) 0.18 (0.07-0.49)]. Side-effects of intrathecal clonidine were not detected [12]. The authors concluded that the addition of clonidine (75 microg) to hyperbaric bupivacaine prolongs spinal anesthesia after cesarean section and improves early analgesia, but does not reduce the postoperative morphine consumption during the first 24 h [12].

Perispinal anesthesia for Caesarean section allows injection of epidural (ED) or intrathecal (i.t.) morphine to provide long-lasting postoperative analgesia. Dualé et al. studied the effects of epidural versus intrathecal morphine for postoperative analgesia after cesarean section [13]. To compare these two routes, a prospective, randomized, double-blinded study of 53 patients undergoing elective Caesarean section was performed. Combined spinal-epidural anesthesia with 6 mg of i.t. hyperbaric bupivacaine plus sufentanil 5 microg, and additional ED lidocaine was used. Additionally, each patient received either 2 mg (2 ml) of ED morphine plus 1 ml of i.t. normal saline (ED group, n=28), or 0.075 mg (1 ml) of i.t. morphine plus 2 ml of ED normal saline (i.t. group, n=25). Additional postoperative analgesia was given in the form of propacetamol and ketoprofen, plus self-administered i.v. morphine [13]. No major respiratory depression occurred. Time to first demand of morphine was similar in the ED (307.5 min) and i.t. (310 min) groups, as was the incidence of side-effects such as sedation, pruritus, nausea, and vomiting. During the first 24 postoperative hours, VAS pain scores were greater in the i.t. group (P=0.032), as was additional morphine consumption (4 vs. 1.5 mg) (P=0.03). The authors concluded that the ED protocol was more effective than the i.t. protocol, whilst side-effects were similar [13].

In conclusion, as the search for optimal analgesia after cesarean section continues, provision of a "stress free" and "pain free" postoperative period in obstetric patients (as true of any surgical patient) should not be overlooked in our clinical daily practice of obstetric anesthesia.

Key points:

1. Postoperative pain leads to patient discomfort, decreased level of satisfaction, prolonged recovery and higher health care cost.
2. Postoperative pain is a potent trigger for stress response.
3. In the parturient inadequate postoperative pain control after cesarean section may interfere with ambulation, breastfeeding and early maternal bonding with the infant.
4. The American Academy of Pediatrics Committee on Drugs lists morphine, fentanyl and butorphanol as maternally administered opioids that are compatible with breastfeeding.
5. Several studies have demonstrated the superiority of nuraxial postoperative analgesia as compared to systemic opioids.
6. Provision of a stress free and pain free postoperative period in obstetric patients should not be overlooked in our clinical daily practice of obstetric anesthesia.

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